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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KOSSON, ROSANNE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/736,899	DEBAD ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36 and 57-59* is/are pending in the application.

4a) Of the above claim(s) *25-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,19-24 and 57-89* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election with traverse of Group I, claims 1-13, and the species of viruses and protein in claims 5, 6, 58 and 59 in the reply filed on May 26, 2005 is acknowledged. Claim 14 has been amended, no claims have been added, and claim 56 has been canceled. Claims 25-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Concerning the restriction requirement, all of Applicants arguments have been considered. They are found to be persuasive with regard to Group II, claims 14-24, but not with regard to Group III, the kit claims, claims 25-36. In Group II, Applicants' election of the species protein in claim 16 is acknowledged. The species election requirement for claims 17 and 18 has been withdrawn. Accordingly, claims 1-24 and 57-59 are examined on the merits herewith.

Concerning restriction between the method of Group I and the kit of Group III, Applicants assert that these groups should be examined together because there is a special technical feature linking these two groups. The instant application, however, is not a national phase of a PCT application filed under 35 USC §371. Thus, invoking a special corresponding technical feature cannot establish unity of invention which would have the two groups examined together. Even the instant application had been filed

under 35 USC §371, the corresponding technical feature of nitrous acid is not novel, i.e., not special, and would not establish unity of invention.

Further, examining Group III along with Group I does create an undue burden of search and examination on the Examiner, because the two searches are not coextensive, and each search has different prior art considerations. Burden lies not only in the search of U.S. patents, but in the search for literature and foreign patents and in examination of the claim language and specification for compliance with the statutes concerning new matter, distinctness and scope of enablement. Claim 25 recites a set of components in one or more containers, a limitation which need not be considered for Group I, and the components of a surfactant, a first binding agent and a second binding agent, additional limitations that need not be considered for Group I.

Applicants also assert that they would need to file a divisional application for the kit claims, that there would be a delay in having these claims examined and that the divisional application would result in inefficiencies and unnecessary expenditures by Applicants. Firstly, these are not criteria pertinent to restriction. Secondly, filing the divisional application is up to Applicants; there need not be a delay. Thirdly, inefficiency and unnecessary expenditures are subjective matters about which the Office does not make a determination. Lastly, as noted above, searching Group I does not cover searching Group III. The restriction requirement is maintained and is made final.

Allowable Subject Matter

Claim 18 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, 19-24 and 57-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the claims recite a method for measuring a plurality of organisms in a sample by measuring markers of the plurality of organisms (claim 1), a method for measuring a plurality of organisms in a sample wherein at least two markers are measured, a streptococcal cell wall-associated antigen and a viral marker (claim 14), a method for measuring two or more markers (claim 57), and a method for measuring one or more markers (claims 58 and 59). Thus, the claims recite methods of measuring at least any two markers, each from a different organism (claim 1) or not necessarily from different organisms (claim 57); methods of measuring any marker from an any organism, if the marker is viral or

protein (claims 58 or 59), and a method of measuring a streptococcal marker and any viral marker (claim 14).

But, the specification discloses only methods in which the Strep A surface antigen, a polysaccharide, is extracted and measured (the non-viral marker) and in which protein surface antigens from Influenza A, Influenza B and Respiratory Syncitial Virus (RSV) are extracted and measured (the viral markers). No other markers are disclosed, except by reference to the prior art (Strep B, Strep C, Strep F and Strep G). There is no evidence that any other representative species of such large and varied genera- markers of organisms and protein viral markers- were in the possession of the inventors at the time of filing. To satisfy the written description aspect of 35 U.S.C. 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed. The specification discloses only Streptococcal cell wall antigens as the organism markers and proteins from Influenza A and B and RSV as the viral markers. Therefore, claims 1-17, 19-24 and 57-59 fail to satisfy the written description requirement.

Claims 1-17, 19-24 and 57-59 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of measuring a plurality of organisms (two or more) in which the organisms are selected from the consisting of Strep A, Strep B, Strep C, Strep F, Strep G, Influenza A, Influenza B and

RSV, by measuring a surface antigen marker of each organism, does not reasonably provide enablement for a method of measuring a plurality of organisms (two or more) in which the organisms may be any two or more organisms, or a method of measuring any two or more markers, or a method of measuring any one marker that is viral or protein, or a method of measuring a streptococcal group-specific antigen and any viral marker. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. More specifically, the specification teaches that a solution containing 1 M nitrite or 2.5 M nitrite can extract antigenic polysaccharides from Streptococci or antigenic proteins from Influenza A and B and RSV. But the specification does not teach that this method can extract surface antigens from any other organisms. Additionally, these strong nitrite solutions may destroy surface antigens from other organisms, even if they could be extracted (i.e., separated from the rest of the cell wall or cell membrane or protein coat). Nitrous acid is an oxidizing acid that reacts with amines and amides to form nitroso compounds. Thus, when treated with nitrite or nitrous acid, an extracted surface antigen may not bind to the antibody or other ligand that the native marker binds to and may no longer be detectable by known detection reagents.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to

practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary (immense, because Applicants assert that the claimed methods can extract and measure for detection any marker from any organism as long as two or more organisms are present in the sample, or any marker from any organism if only one organism is present in the sample as long as the marker is protein or viral, while the specification teaches only that, as means of detecting the presence of a particular organism, 1 M nitrite or 2.5 M nitrite can extract antigenic cell wall polysaccharides from Streptococci or antigenic surface proteins from Influenza A and B and RSV, thereby leaving a large gap in the amount of information provided and the amount of information needed to practice the claimed method, to be filled in by one of ordinary skill in the art),

(2) the amount or direction or guidance presented (methods for extracting cell wall polysaccharides from Streptococci or surface proteins from Influenza A and B and RSV are provided, and the specification notes that these may be detected by commercially available antibodies),

(3) the presence or absence of working examples (working examples are provided for detecting *S. pyogenes* (Group A Strep) alone; Influenza A alone; Influenza A, Influenza B, RSV and Strep A in separate wells of a microtiter plate with a common detection reagent; Influenza A and Strep A mixed together; and Influenza A and Strep A in separate wells of a microtiter plate with a common detection reagent),

(4) the nature of the invention (contacting a sample with a reagent comprising nitrous acid for measuring at least any two markers of an organism; or measuring at least any two markers of at least two organisms; or measuring a viral or protein marker of an organism; or measuring a streptococcal marker and a viral marker),

(5) the state of the prior art (methods of measuring streptococcal group-specific antigens by contacting mixed culture samples containing various Streptococci with a reagent comprising nitrous acid is taught by Bogart et al., US 5,494,801, and Sand et al., US 5,536,646, discussed below),

(6) the relative skill of those in the art (very high, that of highly trained research scientist),

(7) the predictability or unpredictability of the art (see below), and

(8) the breadth of the claims (broad, as discussed above).

With respect to the quantity of experimentation required, many experiments would have to be conducted under a wide range of conditions. In these experiments, samples of a large number of organisms, including a large number of viruses, would each have to be treated with nitrous acid solutions of a large range of concentrations to determine whether or not the nitrous acid solutions could extract an organism-specific

marker without destroying it. The results of the experiments would have to show that a certain range of concentrations of nitrous acid can extract organism-specific markers from a large number of viruses and other organisms and that the extracted markers remain intact so that they can be detected with known detection reagents. If a marker is significantly modified or degraded in the extraction process, one of skill in the art would not know how to prepare a detection reagent to detect the modified or degraded marker.

A great deal of guidance is needed to establish that a nitrous acid-containing extraction reagent can extract markers from any organism, or any virus, because the claims recite measuring any marker from any organism as long as two or more organisms are present in a sample, or measuring any marker from any organism if only one organism is present in the sample as long as the marker is protein or viral. Even if detecting any two markers, or detecting any one viral or protein marker, by nitrous acid extraction can be shown, without a very large amount of data, one of skill in the art would not expect such a result in a sample containing at least one different organism or a sample containing a different virus or organism with a protein marker.

Regarding predictability, because the claimed methods, even when combined with the prior art, have been performed with an extremely limited number of markers (streptococcal, Influenza A, Influenza B and RSV), the allegation that the claimed methods can measure any two markers or any one viral or protein marker by nitrous acid extraction is not supported by the specification. Based on the specification, one of skill in the art would not expect a nitrous acid-containing reagent to be able to extract any two markers or any one viral or protein marker so that one or more particular

organisms in a sample may be identified. Therefore, the claims fail to satisfy the enablement requirement.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7-11, 13, 57 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Bogart et al., US 5,494,801. Bogart et al. disclose a method of measuring two or more markers in a sample containing two or more organisms by first extracting the markers with a solution containing nitrous acid (see col. 1, line 26, to col. 2, line 32). The organisms may be Streptococci of Groups A, B, C, G, or F, and the markers may be polysaccharides, proteins, lipopolysaccharides, lipoproteins or nucleic acid molecules (col. 6, lines 10-18). The sample containing the organisms may contain mucous and may be a genital discharge sample (see col. 10, lines 33-49). The extraction reagent further comprises a surfactant, and following extraction the pH of the assay composition is neutralized (see col. 10, line 59, to col. 11, line 36). The markers are measured in a multiplexed immunoassay format (see col. 13, lines 10-53), as more than one antibody may be added to a test sample to detect more than one organism. Therefore, a holding of anticipation is required.

Claims 1-4, 7, 8, 10, 11, 13 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Slifkin et al., J Clin Micro 12(4):541-545, 1980. Slifkin et al. disclose a method of measuring two or more markers in a sample containing two or more organisms by first transferring patient throat culture samples collected on clinical swabs to blood agar plates. The plates were incubated for colony growth, and, from each plate, a beta-hemolytic colony that was not isolated from background flora was tested for the presence of one or more types of Streptococci (see p. 541, right col., and p. 543, left col.). To prepare cultured colony samples for analysis, the streptococcal markers were extracted with nitrous acid and neutralized (see p. 542, 5th full paragraph). Aliquots of each extracted sample were added to each reagent of a set of reagents containing antibodies to Group A, Group B, Group C and Group G Strep. Each sample was measured for the presence of each antibody to determine the type or types of Strep in the sample (see p. 543, right col.). The markers are measured in a multiplexed immunoassay format, as more than one antibody is contacted with each test sample to detect more than one organism. Therefore, a holding of anticipation is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rosanne Kosson
Examiner
Art Unit 1653

rk/2005-06-15

ROBERT A. WAX
PRIMARY EXAMINER
Art Unit 1653